REMARKS

This Amendment is responsive to the Examiner's Answer dated August 20, 2009 and constitutes a reply under 37 C.F.R. 1.111. In response to the Examiner's Answer, which presented a new ground of rejection, Applicant requests that prosecution be reopened and that the appeal be withdrawn. Reconsideration and withdrawal of the rejection of the claims presented and maintained in the Examiner's Answer are respectfully requested in view of the amendment to the claims presented herein and the following remarks.

Applicant has amended claims 21, 23, and 29, and added claims 47–54. The amendments to the claims are relevant to the new grounds of rejection. Claims 21–24, 26, 29–33, 35–42, and 46–54 will be pending upon entry of this Amendment.

Claim Rejection Under 35 U.S.C. § 102(b)

In the Examiner's Answer, a new ground of rejection was presented in which claims 21, 23, 24, 26, 29–33, and 46 were rejected as being anticipated by Heil, Jr. et al. (U.S. Patent No. 4,819,662, hereinafter "Heil") under 35 U.S.C. § 102(b). Applicant respectfully traverses the rejection of the claims, particularly to the extent such rejection may be considered applicable to the claims as amended. Heil fails to disclose or suggest the inventions defined by Applicant's claims, and provides no teaching that would have suggested the desirability of modification to arrive at the claimed invention.

Applicant has amended independent claim 21 for purposes of clarification. Claim 21 as amended specifies that a medical lead comprises a porous electrode mounted on a lead body to deliver electrical stimulation to a stimulation site within a patient, a genetic material that causes expression of at least one of a connexin or a gap-junction by the tissue at the stimulation site, where the expression of the at least one of the connexin or the gap-junction by the tissue at the stimulation site increases the conductivity of the tissue, and a chamber body that defines a chamber. According to claim 21 as amended, the chamber contains a polymeric matrix that absorbs the genetic material and degrades to elute the genetic material to tissue at the stimulation site via the porous electrode. Support for the amendment to claim 21 can be found throughout Applicant's disclosure, such as at paragraphs [0021] and [0032].

Heil fails to disclose or suggest the lead of Applicant's independent claim 21. For example, Heil does not disclose a lead that includes a genetic material and polymeric matrix that

absorbs the genetic material. Instead, Heil discloses a cardiac pacing lead that includes a porous electrode that dispenses a therapeutic drug.[1]

Heil also fails to disclose or suggest a polymeric matrix that absorbs a genetic material and degrades to elute the genetic material. As acknowledged in the Examiner's Answer, Heil discloses a silicone matrix.[2] Even if silicone is capable of absorbing a genetic material, an assertion with which Applicant does not necessarily agree, Heil fails to disclose or suggest that the silicone is capable of degrading in order to elute a genetic material. Heil states that body fluid flows in and out of the matrix, and that the drug is dispensed from the matrix upon contact with the body fluids.[3] However, Heil does not disclose or even suggest that the silicone matrix degrades in order to elute the drug. The matrix disclosed by Heil is structurally different than the matrix recited in Applicant's claim 21, which absorbs a genetic material and degrades to elute the genetic material. Therefore, the silicone matrix disclosed by Heil cannot reasonably be characterized as the polymeric matrix of Applicant's claim 21.

For at least these reasons, Applicant's independent claim 21 is patentable over Heil under 35 U.S.C. § 102(b). Claims 23, 24, 26, 29–33, and 46 depend from independent claim 21 and are patentable over Heil for at least the reasons discussed with respect to claim 21. Reconsideration and withdrawal of the rejection to claims 21, 23, 24, 26, 29–33, and 46 are respectfully requested.

Claim Rejection Under 35 U.S.C. § 103(a)

In the Examiner's Answer, a new ground of rejection was presented in which claim 22 was rejected as being obvious over Heil in view of Soykan et al. (U.S. Patent No. 6,151,525, hereinafter "Soykan") under 35 U.S.C. § 103(a).[4] In addition, the Examiner maintained the rejection of claims 21–24, 26, 29–33, 35–42 and 46 under 35 U.S.C. § 103(a) as being unpatentable over Soykan in view of Heil and Girouard et al. (U.S. Patent Application Publication No. 2004/0158289, hereinafter "Girouard").

[1] Heil, Abstract.
[2] Examiner's Answer dated August 2, 2009, page 5; Heil, col. 4, ll. 45–49.
[3] Heil, col. 2, ll. 17–21 and col. 7, ll. 14–17.
[4] Examiner's Answer dated August 20, 2009, page 2.

Applicant respectfully traverses the rejection of the claims. The applied references fail to disclose or suggest the inventions defined by Applicant's claims, and provide no teaching that would have suggested the desirability of modification to arrive at the claimed invention.

Rejection of Claim 22 Based on Heil in View of Soykan

With respect to claim 22, for example, Heil in view of Soykan fails to disclose or suggest a medical lead that includes a chamber body that defines a chamber that contains a polymer matrix comprising extracellular collagen. The Examiner's Answer acknowledged that Heil fails to disclose or suggest a matrix that comprises extracellular collagen, and looked to Soykan to cure this deficiency in Heil. The Examiner's Answer asserted that it would have been obvious to modify Heil in view of Soykan to provide "the predictable result of a natural drug delivery material that allows for controlled chronic drug or genetic material delivery."[5] Applicant respectfully disagrees with the conclusion of obviousness presented in the Examiner's Answer.

A matrix comprising extracellular collagen is a biological matrix that necessarily has different properties than non-biological silicone, the matrix material disclosed by Heil. Therefore, contrary to the assertions in the Examiner's Answer, the results of substituting collagen for silicone in the matrix disclosed by Heil are not predictable. Indeed, substituting a matrix comprising collagen for the silicone matrix disclosed by Heil, as proposed in the Examiner's Answer, would not have yielded predictable results.[6] For example, the mechanisms by which silicone and collagen absorb and elute materials substantially differ, such that the manner in which the collagen would be loaded with the drug disclosed by Heil and elute the drug is unclear.

The Examiner's Answer asserted that Soykan "teaches that it is known in the art to elute drugs and genetic material using extracellular collagen."[7] However, Soykan only discloses the use of a polymeric matrix comprising collagen to deliver a genetic material. Soykan does not disclose or suggest that the collagen is suitable for delivering a drug. Indeed, the molecular structure of genetic material and a drug can differ greatly, such that the use of the matrix comprising collagen disclosed by Soykan in place of the matrix comprising silicone disclosed by Heil would not have been obvious. For example, genetic material can have a larger molecular

[5] Examiner's Answer dated August 20, 2009, page 6.
[6] *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007).
[7] Examiner's Answer dated August 20, 2009, page 6.

weight than a drug. As a result, the materials selected for the matrices that are used to deliver the genetic material can differ from the materials selected from the matrices that are used to deliver a drug.

Even in the case of a claim rejection based on the "predictable results" rationale, identification of a reason why a person of ordinary skill would have combined the elements in the manner proposed by the Examiner is important.[8] The Examiner failed to identify a rational reason why a person of ordinary skill would have modified the Heil polymeric matrix with the polymeric matrix comprising collagen disclosed by Soykan. Therefore, the Examiner failed to establish a *prima facie* case of obviousness with respect to claim 22.

Neither Heil nor Soykan disclose or suggest that a matrix including silicone and a matrix including collagen elute a drug in the same manner. As a result, the references fail to provide any support for a reasonable expectation that a matrix comprising collagen would successfully elute the drug disclosed by Heil. For example, the cited references fail to disclose or even suggest that collagen is capable of providing the "free fluid flow" out of the recess in the lead, as required by Heil.[9] As a result, there is no rational basis for asserting that one having ordinary skill in the art would have modified Heil to include the matrix comprising collagen disclosed by Soykan.

For at least these reasons, Applicant's claim 22 is patentable over Heil in view of Soykan.

Rejection of Claims 21–24, 26, 29–33, 35–42 and 46 Based on Soykan in View of Heil and Girouard

Claims 21–24, 26, 29–33, 35–42 and 46 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Soykan in view of Heil and Girouard. Applicant respectfully traverses the rejection of the claims as being obvious over Soykan in view of Heil and Girouard. For at least the reasons presented in the Appeal Brief filed on May 8, 2009, Soykan in view of Heil and Girouard lacks any teaching that would have suggested the medical lead of Applicant's independent claim 21 or the method of Applicant's independent claim 35. For example, Soykan in view of Heil and Girouard fails to disclose or suggest a medical lead that includes a matrix that elutes a genetic material that is adapted to cause expression of at least one of a connexin or a

[8] MPEP 2143, *citing KSR Int'l Co.*, 550 U.S. at 418.
[9] Heil, col. 2, ll. 34–40.

gap-junction by the tissue at the stimulation site, whereby the matrix elutes the genetic material to the stimulation site via a porous electrode of the lead.

The Examiner's Answer provided a clarification of the rejection of claims 21–24, 26, 29–33, 35–42 and 46 under 35 U.S.C. § 103(a) as being unpatentable over Soykan in view of Heil and Girouard. For example, the Examiner's Answer asserted that one having ordinary skill in that art would have modified Soykan to include elute a genetic material via the porous electrode disclosed by Heil "because the cells that are the target of the therapeutic agent are the same cells that are the target of the electrical therapy" in Soykan, and, therefore, one having ordinary skill in the art would have been motivated "to provide the agent *at the site of electrical therapy.*"[10] This rationale, however, is based on an unsupported assumption that the electrical therapy disclosed by Soykan would still be desirable after modification of Soykan in view of Heil to include the genetic material disclosed by Girouard.

Soykan discloses the use of genetic material to convert noncontracting cells to contracting cells in an infarct zone of a patient's myocardium.[11] Soykan discloses the delivery of stimulation to tissue for a very specific purpose, i.e., in order to make newly formed contractile tissue beat in synchrony with the rest of the heart muscle.[12] Girouard does not disclose that biological conditioning with a transgene that encodes connexin increases contractility of tissue, such that electrical therapy is desirable. Girouard discloses a transgene that encodes, e.g., connexin-40, connexin-42, and connexin-43, to condition donor cells *in vitro*.[13] In particular, Girouard uses the genetic material to subject donor cells to exogenous agents, such as differentiation factors, growth factors, and the like.[14] Girouard does not disclose or suggest that electrical therapy is necessary or even desirable upon the biological conditioning with a transgene that encodes connexin. Therefore, the rationale proposed in the Examiner's Answer for modifying Soykan in view of Heil and Girouard in order "to provide the agent *at the site of electrical therapy*"[15] lacks a rational underpinning.

The Examiner's Answer also address Applicant's position in the Appeal Brief that the use of genetic material to condition exogenous cells by Girouard is contrary to Soykan, which

[10] Examiner's Answer dated August 20, 2009, pages 10 and 11 (emphasis in original).
[11] Soykan, col. 7, ll. 54–60.
[12] Soykan, col. 13, ll. 11–15.
[13] Girouard, ¶¶ [0076], [0129], and [0146].
[14] Girouard, ¶ [0146].
[15] Examiner's Answer dated August 20, 2009, pages 10 and 11 (emphasis in original).

discloses the conversion of cells in an infarct zone within the patient using genetic material.[16] The Examiner's Answer stated that paragraph [0044] of "Girouard recognizes that the vectors may be applied either *in vitro* or *in vivo*."[17] At paragraph [0044], Girouard provides a general definition for a "vector," and states that the "vector" can be a macromolecule or a complex of molecules comprising a polynucleotide to be delivered to a host cell *in vitro* or *in vivo*. With respect to the specific examples relating to a transgene that encodes connexin, however, Girouard does not state that the encoding of connexin can take place *in vivo*. Instead, Girouard discloses a transgene that encodes, e.g., connexin-40, connexin-42, and connexin-43, to condition donor cells *in vitro*, prior to administration of the donor cells into a region of injured tissue of the patient.[18] The donor cells are conditioned outside of the patient, and then subsequently introduced into the tissue region to be treated. Thus, Girouard is only directed to the use of exogenous cells[19] that may be conditioned using genetic material.

The use of genetic material to condition exogenous cells by Girouard is contrary to Soykan, which discloses the conversion of cells in an infarct zone within the patient using genetic material. As discussed in further detail in the Appeal Brief, neither Soykan nor Girouard provides any indication that the encoding of connexin, which takes place *ex vivo* in the Girouard reference, may be simply substituted in the *in vivo* technique disclosed by Soykan, as asserted by the Examiner.[20]

The Examiner's Answer also asserted that Girouard discloses "specific genetic material recognized as useful for improving cardiac tissue contractility."[21] Girouard, however, does not disclose or suggest that a genetic material that encodes connexin improves cardiac tissue contractility. Girouard states that mechanical conditioning of donor cells (e.g., subjecting donor cells to a mechanical stress) "can result in donor cells that are capable of contracting upon excitation by action potentials"[22] and that delivery of electrical therapy can enhance contractile function of cells.[23] Girouard also discloses transgenes that encode a gene product including

[16] *See* Appeal Brief filed May 8, 2009 at page 10.
[17] Examiner's Answer dated August 20, 2009, page 12.
[18] Girouard, ¶¶ [0076], [0129], and [0146].
[19] Girouard, Abstract.
[20] Final Office Action dated January 23, 2009, p. 6, item 13 (Response to Arguments section).
[21] Examiner's Answer dated August 20, 2009, page 12.
[22] Girouard, paragraph [0131].
[23] Girouard, paragraph [0075].

contractable proteins.[24] The encoding of contractable proteins, however, is different than the encoding of connexin. Moreover, Girouard does not state that the contractable proteins improve cardiac tissue contractility. Furthermore, Girouard does not state that genetic material that causes encoding of connexin improves cardiac tissue contractility.

Girouard discloses *in vitro* conditioning of donor cells in order to augment or replace cardiac muscle.[25] On the other hand, Soykan discloses an *in vivo* technique for converting noncontracting cells to contracting cells. Contrary to the assertions in the Examiner's Answer, there is no rational reason why one having ordinary skill in the art would have modified Soykan in view of Heil in further view of Girouard to deliver the genetic material disclosed by Girouard, which encodes connexin-40, connexin-42, and connexin-43, *in vivo*. Without access to Applicant's disclosure, one having ordinary skill in the art would not have looked to substitute the genetic material disclosed by Soykan with the genetic material disclosed by Girouard, which is only disclosed as being used to provide *in vitro* conditioning of donor cells.

Neither Soykan nor Girouard provides any indication that expression of connexin, which takes place *ex vivo* in the Girouard reference, may be simply substituted in the *in vivo* technique disclosed by Soykan, as asserted by the Examiner.[26] Even if the genetic material disclosed by Girouard could have been "predictably applied" to the Soykan system,[27] as asserted in the Examiner's Answer, identification of a reason why a person of ordinary skill would have combined the elements in the manner proposed by the Examiner is important.[28] However, the Examiner has failed to identify any rational reason for the modification. Moreover, as discussed in further detail in the Appeal Brief, the combination of Soykan, Heil, and Girouard proposed by the Examiner changes the established functions of the cited references.[29] Therefore, Applicant's claims are not obvious in view of the cited references.[30]

For at least these reasons and the reasons discussed in the Appeal Brief, Applicant's claims 21–24, 26, 29–33, 35–42 and 46 are patentable over the cited references under 35 U.S.C. § 103(a). Reconsideration and withdrawal of the rejection of the claims are respectfully requested.

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[24] Girouard, paragraph [0146].
[25] Girouard, paragraph [0074].
[26] Final Office Action dated January 23, 2009, p. 6, item 13 (Response to Arguments section).
[27] Applicant respectfully disagrees with this assertion.
[28] MPEP 2143, *citing KSR Int'l Co.*, 550 U.S. at 418.
[29] Appeal Brief filed May 8, 2009, page 11.
[30] *See* MPEP 2141, *citing KSR Int'l Co.*, 550 U.S. at 417.

New Claims

Applicant has added claims 47–54 to the pending application. The applied references fail to disclose or suggest the inventions defined by Applicant's new claims, and provide no teaching that would have suggested the desirability of modification to arrive at the claimed inventions. No new matter has been added by the new claims.

CONCLUSION

All claims in this application are in condition for allowance. Applicant respectfully requests reconsideration and prompt allowance of all pending claims. In view of the fundamental differences identified above, Applicant reserves further comment concerning the additional features set forth in the dependent claims. However, Applicant does not acquiesce in the propriety of the application or interpretation of the prior art presented in the Office Action with respect to the dependent claims, and reserves the right to present additional arguments in any further prosecution of this application.

Please charge any additional fees or credit any overpayment to deposit account number 50-1778. The Examiner is invited to telephone the below-signed attorney to discuss this application.

Date: October 20, 2009

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